I. AMENDMENT

In the specification:

Please replace paragraph 18, beginning at page 9, with the following rewritten paragraph:

--Preferred heterodimerization sequences contained in the subject antigen-binding units are derived from C-terminal sequences of $GABA_B$ receptor 1 and $GABA_B$ receptor 2, respectively. More preferably, the first heterodimerization sequence is linked to a cysteine residue, said first heterodimerization comprising a $GABA_B$ receptor 1 polypeptide of at least 30 amino acid residues that is essentially identical to a linear peptide sequence of comparable length depicted in SEQ ID NO. 2; and the second heterodimerization sequence is linked to a cysteine residue, said second heterodimerization comprising a $GABA_B$ receptor 2 polypeptide of at least 30 amino acid residues that is essentially identical to a linear peptide sequence of comparable length depicted in SEQ ID NO. 4. Alternatively, the first heterodimerization sequence is linked to a cysteine residue, said first heterodimerization comprising a $GABA_B$ receptor 2 polypeptide of at least 30 amino acid residues that is essentially identical to a linear peptide sequence of comparable length depicted in SEQ ID NO. 4; and the second heterodimerization sequence is linked to a cysteine residue, said second heterodimerization comprising a $GABA_B$ receptor 1 polypeptide of at least 30 amino acid residues that is essentially identical to a linear peptide sequence of comparable length depicted in SEQ ID NO. 2.--

A1

Please replace paragraph 37, beginning at page 13, with the following rewritten paragraph:

--Figure 2 depicts the nucleotide and amino acid sequences of $GABA_B$ receptor 1 and 2 that were used in constructing the subject Abus. The coiled-coil sequences are derived from human $GABA_B$-R1 and $GABA_B$-R2 receptors. The coding amino acid sequences from $GABA_B$ receptor 1 begins with EEKS and ends with QLQS as shown in the top panel of Figure 2 . The coding amino acid sequences from $GABA_B$ receptor 2 begins with TSRL and ends with QLQD as shown in the bottom panel of Figure 2 . A flexible SerArgGlyGlyGlyGly spacer was added to the amino-termini of R1 and R2 heterodimerization sequences to favor the formation of functional Fv heterodimer. To further stabilize the heterodimer, we have introduced a ValGlyGlyCys spacer to lock the heterodimeric coiled-coil pair via the disulfide bond between the cysteine residues (SEQ ID NOS. 2 and 4). The SerArg coding sequences at the N-terminus of the GGGG spacer provides XbaI or XhoI sites for fusion of the GR1 (heterodimerization sequence derived from $GABA_B1$ receptor) and GR2 (heterodimerization sequence derived from $GABA_B2$) domains to the carboxyl-termini of VH and VL fragments, respectively.--

A2

Please replace the title at page 49 with the following rewritten title:

--**Polynucleotides and Vectors of the Present Invention**--

Please replace paragraph 75, beginning at page 23, with the following rewritten paragraph:

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--"Single-chain antigen-binding unit" ("Sc Abu") refers to a monomeric Abu. Although the two domains of the Fv fragment are coded for by separate genes, a synthetic linker can be made that enables them to be made as a single protein chain (i.e. single chain Fv ("scFv") as described in Bird *et al.* (1988) *Science* **242**:423-426 and Huston *et al.* (1988) *PNAS* 85:5879-5883) by recombinant methods. Other Sc Abus include antigen-binding molecules stabilized by the subject heterodimerization sequences (see e.g. Figure 18), and dAb fragments (Ward *et al.*, (1989) *Nature* **341**:544-546) which consist of a VH domain and an isolated complimentarity determining region (CDR). An example of a linking peptide is $(GGGGS)_3$, which bridges approximately 3.5 nm between the carboxyl terminus of one V region and the amino terminus of another V region. Other linker sequences can also be used, and can provide additional functions, such as a means for attaching a drug or a solid support. A preferred single-chain antigen-binding unit contains VL and VH regions that are linked together and stabilized by a pair of subject heterodimerization sequences. The scFvs can be assembled in any order, for example, VH—(first heterodimerization sequence)-(second heterodimerization sequence) —VL, or V_L—(first heterodimerization sequence)-(second heterodimerization sequence) —VH.--

Please replace paragraph 105, beginning at page 32, with the following amended paragraph:

A4

--As noted above, proper assembly of polypeptide subunits to form a stable complex is required to ensure the biological function of a multimeric protein. Accordingly, a central aspect of the present invention is the design of a technique that enables specific assembly of selected monomeric polypeptides to effect efficient production of heteromultimers. The experimental design is particularly useful for generating and screening for heteromultimers such as Abus whose binding specificities depend on the assembly of specific subunits in a specific manner. Distinguished from the previously reported chimeric Abus, the subject Abus have one or more of the following unique features. First, the Abus are reconstituted via pairwise affinity of two heterodimerization sequences, at least one of which and preferably both of which, lack(s) detectable propensity to form homodimers. Unlike the previously reported dimerization sequences such as *Fos* and *Jun* leucine zippers that are known to form homodimers under both physiological buffer conditions and physiological body temperature (O'Shea *et al.* (1992) *Cell* **68**: 699-708; Vidal *et al.* (1996) *Proc. Natl. Acad. Sci. U.S.A*), the subject heterodimerization sequences are essentially incapable of forming homodimers either under the specified buffer conditions and/or at the specified

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body temperatures. The subject heterodimerization sequences may be also distinguished from the previously employed sequences at the structural level as detailed below.

Please replace paragraph 106, beginning at page 32, with the following amended paragraph:

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In one embodiment, the present invention provides a chimeric ~~heteromultimer~~ displayed on the surface of the host cell, wherein heteromultimer comprises: (i) a first polypeptide fused to a first heterodimerization sequence and a surface presenting sequence; (ii) a second polypeptide fused to a second heterodimerization sequence; wherein the first and second polypeptides dimerize via pairwise affinity of the first and second heterodimerization sequences; wherein at least one of the heterodimerization sequences is essentially incapable of forming a homodimer under physiological buffer conditions and/or at physiological body temperatures.

Please replace paragraph 110, beginning at page 35, with the following amended paragraph:

A6

Second, the selected heterodimerization sequences must exhibit pairwise affinity resulting in predominant formation of heterodimers to a substantial exclusion of homodimers. Preferably, the predominant formation yields a heteromultimeric pool that contains at least 60% heterodimers, more preferably at least 80% heterodimers, more preferably between 85-90% heterodimers, and more preferably between 90-95% heterodimers, and even more preferably between 96-99% heterodimers that are allowed to form under physiological buffer conditions and/or physiological body temperatures. In certain embodiments of the present invention, at least one of the heterodimerization sequences employed to reconstitute an Abu is essentially incapable of forming a homodimer in a physiological buffer and/or at physiological body temperature. By "essentially incapable" is meant that the selected heterodimerization sequences when tested alone do not yield detectable amounts of homodimers in an *in vitro* sedimentation experiment as detailed in Kammerer *et al.* (1999) *Biochemistry* 38: 13263-13269), or in the *in vivo* two-hybrid yeast analysis (see e.g. White *et al. Nature* (1998) 396: 679-682). Specifically, Kammerer et al. have demonstrated by sedimentation experiments that the heterodimerization sequences of $GABA_B$ receptor 1 and 2, when tested alone, sediment at the molecular mass of the monomer under physiological conditions and at physiological body temperatures (e.g. at 37^0C). When mixed in equimolar amounts, $GABA_B$ receptor 1 and 2 heterodimerization sequences sediment at the molecular mass corresponding to the heterodimer of the two sequences (see Table 1 of Kammerer et al.). In addition, individual heterodimerization sequences can be expressed in a host cell and the absence of homodimers in the host cell can be demonstrated by a variety of protein analyses including but not limited to SDS-PAGE, Western blot, and immunoprecipitation. The *in vitro* assays must be conducted under a

physiological buffer conditions, and/or preferably at physiological body temperatures. Generally, a physiological buffer contains a physiological concentration of salt and at adjusted to a neutral pH ranging from about 6.5 to about 7.8, and preferably from about 7.0 to about 7.5. A variety of physiological buffers is listed in Sambrook *et al.* (1989) *supra* and hence is not detailed herein. Preferred physiological conditions are described in Kammerer *et al.*, *supra*.--

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Please replace paragraph 119, beginning at page 40, with the following amended paragraph:

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--While a diverse variety of coiled coils involved in hetero-oligomerization can be employed in the subject invention, preferred coiled coils are derived from heterodimeric receptors. Accordingly, the present invention encompasses the coiled-coil dimeric sequences derived from $GABA_B$ receptors 1 and 2. In one aspect, the subject coiled coils comprise the C-terminal sequences of $GABA_B$ receptor 1 and $GABA_B$ receptor 2. In another aspect, the subject coiled coils are further linked to cysteine residues. The coiled coils are $GABA_B$ receptor 1 and 2 polypeptides of at least 30 amino acid residues, one of which is essentially identical to a linear sequence of comparable length depicted in SEQ ID NO. 2, and the other is essentially identical to a linear peptide sequence of comparable length depicted in SEQ ID NO. 4.--

Please replace paragraph 167, beginning at page 58, with the following amended paragraph:

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--In constructing the subject vectors, the termination sequences associated with the exogenous sequences are also inserted into the 3' end of the sequence desired to be transcribed to provide polyadenylation of the mRNA and/or transcriptional termination signal. The terminator sequence preferably contains one or more transcriptional termination sequences (such as polyadenylation sequences) and may also be lengthened by the inclusion of additional DNA sequence so as to further disrupt transcriptional read-through. Preferred terminator sequences (or termination sites) of the present invention have a gene that is followed by a transcription termination sequence, either its own termination sequence or a heterologous termination sequence. Examples of such termination sequences include stop codons coupled to various polyadenylation sequences that are known in the art, widely available, and exemplified below. Where the terminator comprises a gene, it can be advantageous to use a gene which encodes a detectable or selectable marker; thereby providing a means by which the presence and/or absence of the terminator sequence (and therefore the corresponding inactivation and/or activation of the transcription unit) can be detected and/or selected.--